(II) Claim 2 has been amended to use proper Markush claim format, in accord with the Examiner's suggestion.

(III) Claims 6-8 and 16-17 are rejected because of the use of trademarks in the claims, and claims 16-17 are rejected for the use of the term "Neutres." Reference to Aquacoat®, Eudragit NE®, and Neutres has been replaced with the generic description of these compounds. See page 4 of the specification, for example.

(IV) Claim 4 is rejected for the use of the term "such as," which has been clarified by the present amendment of claim 4 and the addition of claim 21.

(V) Claim 14 is rejected because it is unclear to what the phrase "30-40%" refers. The claim is amended to recite that this is a volume/volume percentage of alcohol. See the top of page 6 of the specification, for example (at "aqueous-alcoholic solution").

(VI) Claim 10 (inadvertently identified as claim 14) is rejected because is it unclear to what "0.1 mg/g and 750 mg/g" refers. The claim is amended to recite that this number refers to the weight of plant substance relative to the total weight of the granule, as is supported throughout the specification.

(VII) Claim 11 is rejected as missing a recitation of a positive method step. The amended claim recites the method step of coating the neutral core with a layer containing a plant substance combined with a pharmaceutically acceptable excipient. The claim now provides a positive method step, and the rejection should be withdrawn.

(VIII) Claims 16-17 are rejected because the term "Neutres" lacks antecedent basis. The claims are amended to provide a generic description of Neutres, as indicated above, and the rejection accordingly may be withdrawn.

The claims, thus amended, comply with Section 112, second paragraph, and the rejections accordingly should be withdrawn.

Rejections under 35 U.S.C. § 102:

(I) Claims 1, 5, 9, and 11-12 are rejected under 35 U.S.C. § 102(b) as anticipated by WO 97/04861 ('861). Applicants traverse the rejection.

To properly anticipate a claim under Section 102, a reference must disclose each and every aspect of the claim. '861 discloses solid granules, which are homogenous from the center to the periphery (see page 3, lines 27-29: "*le granule est homogène dans sa composition, du centre à la périphérie, quelle que soit la taille.*"). By contrast, the claimed granules comprise a neutral core coated with a layer containing the plant substance combined with a pharmaceutically acceptable excipient. '861 does not disclose every element of the claimed invention, and the rejection accordingly is improper and should be withdrawn.

(II) Claims 1-15 are rejected under 35 U.S.C. § 102(b) as anticipated by U.S. Pat. No. 5,733,551 ("Jacob"). Applicants traverse the rejection.

Jacob discloses a process of extrusion and spheronization to prepare an orally absorbable spheroid containing an active ingredient. The products obtained by this method are homogenous. By contrast, the claimed granules comprise a neutral core coated with a layer containing the plant substance combined with a pharmaceutically acceptable excipient. Jacob does not disclose every element of the claimed invention, and the rejection accordingly is improper and should be withdrawn.

(III) Claims 1-3 and 9-15 are rejected under 35 U.S.C. § 102(e) as anticipated by U.S. Pat. No. 6,030,621 ("De Long"). Applicants traverse the rejection.

De Long discloses a pharmaceutical composition comprising Ginkgo biloba. The Examiner cites passages that describe the preparation of Ginkgo biloba extract and the formulation of the extract as a "granule," containing the various other components listed at column 19, lines 65-67. De Long provides no information of the granules' structure or preparation. In particular, De Long nowhere teaches or suggests that the granules comprise a neutral core having a particle size of between 200 and 1600 μm coated with a layer containing the plant substance combined with a pharmaceutically acceptable excipient, as claimed. In the absence of such information, the Examiner can only presume what is the inherent granular

structure; however, it is well established that the Examiner must shoulder the burden of providing evidence that a property allegedly inherent in the prior art **necessarily** flows from the art teachings. As the Examiner's own reviewing court has held, inherency "may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Oelrich*, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981). Accordingly, De Long neither teaches nor suggests the claimed invention, and De Long provides insufficient disclosure to presume that the granules containing Ginkgo biloba extract anticipate the presently claimed invention. The rejection thus is improper and should be withdrawn.

Rejection under 35 U.S.C. § 103(a):

Claims 1-20 are rejected under 35 U.S.C. § 103(a) as obvious over De Long in view of U.S. Pat. No. 6,120,802 ("Breitenbach"). Applicants traverse the rejection.

The teachings of De Long are set forth above. Breitenbach teaches multi-layer medicaments, preferably comprising two or three layers, where at least one layer contains a pharmaceutically active ingredient. See column 2, lines 59-65. The Examiner relies on Breitenbach's description of additives and the use of coating pans and fluidized beds. Breitenbach does not make up for the deficiency of De Long, because he does not describe or suggest using the claim element of a granule comprising a neutral core having a particle size of between 200 and 1600 μm coated with a layer containing the plant substance combined with a pharmaceutically acceptable excipient. Thus, neither of the references suggest that claimed invention. Absent such a suggestion, a proper *prima facie* case of obviousness has not been made, and the rejection accordingly should be withdrawn.

The Examiner proposes "incorporat[ing] the plasticizer and binders taught by Breitenbach into De Long's Ginkgo biloba (a plant substance) granules, and then apply coating on them . . . to formulate a multi layer controlled release formulation . . . ." Such a method would produce granules with the active substance in the internal layer of the granule; however, in the claimed invention, the granules comprise a neutral core coated with a layer containing the plant substance combined with a pharmaceutically acceptable excipient. For

this reason, as well, the rejection is improper and should be withdrawn.

CONCLUSION

In view of the foregoing, it is respectfully urged that the present claims are in condition for allowance. An early notice to this effect is earnestly solicited. If any additional extensions of time are required for the filing of this paper, applicant expressly petitions for such extensions and authorize the Commissioner to charge any deficiency to Deposit Account 19-0741.

Should there be any questions regarding this application, especially if the Examiner feels that he would benefit from further clarification of the invention, the Examiner is encouraged to contact the undersigned at the telephone number shown below.

Respectfully submitted,

March 20, 2001

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Marked-up copy of the pending claims as amended

1. (Amended) Granules containing at least one plant substance, [characterized in that that each comprise] comprising a neutral core having a particle size of between 200 and 1600 µm coated with a layer containing the plant substance combined with a pharmaceutically acceptable excipient.

2. (Amended) Granules according to [Claim] claim 1, [characterized in that] wherein the neutral core consists of a substance [chosen from] selected from the group consisting of sugar, starch, mannitol, sorbitol, xylitol, cellulose, talc, and mixtures thereof.

3. (Twice amended) Granules according to [Claim] claim 1, [characterized in that] wherein the neutral core consists of a starch/sucrose core in a 20/80 mass [ratios] ratio, which is coated with 80% by weight of starch.

4. (Twice amended) Granules according to [Claim] claim 1, [characterized in that] wherein the layer containing the plant substance contains a binder [such as sucrose, polyvinylpyrrolidone, lac gum or hydroxypropylmethylcellulose].

5. (Twice amended) Granules according to [Claim] claim 1, [characterized in that] wherein the layer containing the plant substance is coated with an outer layer [intended to mask the taste and/or the odour] capable of masking the taste or odor of the plant substance[, to delay its release or to control its release].

6. (Amended) Granules according to [Claim] claim 5, [characterized in that] wherein the outer layer is [intended to control] capable of controlling the release of the plant substance and contains lac gum, PVP, a copolymer of methacrylic acid or a colloidal dispersion of ethylcellulose [of Aquacoat®] with a plasticizer.

7. (Amended) Granules according to [Claim] claim 5, [characterized in that] wherein the outer layer is [intended to delay] capable of delaying the release of the plant substance and

contains a copolymer of methacrylic acid, lac gum or a colloidal dispersion of ethylcellulose [Aguacoat®] with a plasticizer.

8. (Amended) Granules according to [Claim] claim 5, [characterized in that] wherein the outer layer is [intended to mask the taste and/or the odour] capable of masking the taste or odor of the plant substance and contains [Eudragit NE30D®, Eudragit E 100®] a copolymer of methacrylic acid or hydroxypropylmethylcellulose.

9. (Twice amended) Granules according to [Claim] claim 1, [characterized in that] wherein the plant substance is selected from the group consisting of garlic, Echinacea, Ginko biloba, ginseng, Harpagpphytum, kava, St,-John's-wort, green tea, valerian, Missouri grape, artichoke, hawthorn, burdock, birch, alder buckthorn, blackcurrant, blessed thistle, Fucus, Hamamelis, horse chestnut, balm, Orthosiphon, passion flower, dandelion, horsetail, meadowsweet, sage, spirulina and mixtures thereof.

10. (Twice amended) Granules according to [Claim] claim 1, [characterized in that] wherein the content of plant substance is between 0.1 mg/g and 750 mg/g weight of plant substance to the total weight of the granule.

11. (Twice amended) [Process for the preparation of] A method of preparing granules comprising coating a neutral core having a particle size of between 200 and 1600 μm [coated] with a layer containing a plant substance combined with a pharmaceutically acceptable excipient, wherein the plant substance coated onto the neutral cores is in the form of a dry, soft or fluid extract.

12. (Amended) [Process of preparation according to Claim] The method according to claim 11, [characterized in that] wherein the granules are obtained by powder-coating when the plant substance is in the form of a dry extract.

13. (Amended) [Process according to Claim] The method according to claim 11, [characterized in that] wherein the granules are obtained by coating in solution when the plant

substance is in the form of a soft or fluid extract.

14. (Amended) [Process according to Claim] The method according to claim 13, [characterized in that] wherein the fluid extract contains from 30 to 40% (v/v) alcohol.

15. (Twice amended) [Process according to Claim] The method according to claim 11, [characterized in that] wherein 5 to 25% by weight of organic solvents are used.

16. (Twice amended) [Process according to Claim] The method according to claim 11, [characterized in that] wherein the size of the [Neutres] neutral core is between 950 and 1400 μm, [when] and wherein the plant extract is dry.

17. (Twice amended) [Process according to Claim] The method according to claim 11, [characterized in that] wherein the size of the [Neutres] neutral core is between 900 and 1250 μm, [when] and wherein the plant extract is soft or fluid.

18. (Twice amended) [Process according to Claim] The method according to claim 11, [characterized in that] wherein the percentage by mass of fluid extract used is between 15 and 25% relative to the weight of the granules.

19. (Twice amended) [Process according to Claim] The method according to claim 11, [characterized in that] wherein the percentage by mass of dry extract [used may be] is as high as 75% relative to the weight of the granules.

20. (Twice amended) [Process according to Claim] The method according to claim 11, [characterized in that] wherein the granules are prepared in a pan or in a fluidized air bed.